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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/662,345	09/16/2003	Levon Arakelyan	Q71975	2068

23373 7590 08/02/2006

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EXAMINER
CLOW, LORI A

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 08/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/662,345	ARAKELYAN ET AL.	
	Examiner	Art Unit	
	Lori A. Clow, Ph.D.	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *10 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11 and 13-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 September 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/6/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election without traverse of Species II (prediction of efficacy, claims 11 and 13) in the reply filed on 20 April 2006 is acknowledged.

Claims 10 and 12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim.

Applicant timely traversed the restriction (election) requirement in the reply filed on 20 April 2006.

Claims 1-17 are currently pending. Claims 10 and 12 have been withdrawn.

Priority

Priority to US Provisional Application 60/410,803, filed 16 September 2002 is hereby acknowledged.

Information Disclosure Statement

The Information Disclosure Statement filed 6 January 2004 has been partially considered. References 1 and 22 have not been considered, as they lack a publication date. A signed copy of PTO Form 1449, including lined through references 1 and 22 is included in with this Office Action.

Drawings

The drawings filed 16 September 2003 are not accepted. Figures 5D, 5I, and 6 are too dark to read legibly. Correction is required.

Abstract

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of **50 to 150 words**. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc. In the instant case, the abstract contains more than 150 words.

Specification

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. For example, see page 1, paragraph [3].

Claim Rejections - 35 USC § 112-1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, 11, and 13-17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of performing interactive clinical trials for testing a new drug for cancer related studies, does not reasonably provide enablement for method of performing interactive clinical trials for testing a new drug for any know n disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use or make the invention commensurate in scope with these claims.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must be able to perform the interactive clinical trials for testing a new drug for any known disease. As will be outlined below, this constitutes undue experimentation.

b) and c) The specification provides examples for performing such a method in the scope of cancer related studies. For example, the specification discloses, at paragraph [52] that "these include the data of experiments using different tumor types". At paragraph [53] the specification teaches that "this again includes data on different tumor types". The specification states at

paragraph [67] that "at this point many simulations are carried out on different cancer types in order to find the optimum protocol for different patient populations".

d) The invention is drawn to methods for performing the interactive clinical trials on any disease. However, the specification is enabled only for performing these methods for cancer.

e) and g) It would have been well known in the art that performing computer modeling is specific for various diseases, based upon the databases that are being employed. For instance, efficacy modeling for tumors would follow a different mathematical protocol from that of modeling for another disease, such as diabetes, for example. Iliadis et al. (Computers and Biomedical Research (2000) Vol. 33, pages 211-226; PTO 1449 reference 30). Teach a specific algorithm to assess tumor growth, in which efficacy is measured. The instant specification is drawn to cancer modeling and therefore, cancer modeling is enabled.

f) The skill of those in the art of molecular biology/bioinformatics is high.

h) The claims are broad because they are drawn to a method applicable to any and all diseases. The skilled practitioner would first turn to the instant specification for guidance to practice methods. However, the instant specification is enabled only for cancer related embodiments. As such, the skilled practitioner would turn to the prior art for such guidance, however, the prior art shows that tumor biology and efficacy modeling is specific. Finally, said practitioner would turn to trial and error experimentation. Such represents undue experimentation.

Claim Rejections - 35 USC § 112-2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9, 11, and 13-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, step (a) recites "performing a preclinical phase in which a computer model for pk/pd of the drug is created and adjusted based upon in vitro and in vivo studies in animals". It is unclear as to what the model is based upon about these particular studies? Is it based upon drug interactions that up regulate or down regulate cells in vivo, for example. What exactly constitutes the model? Clarification is requested.

Claim 1, step (b) recites "performing a phase I clinical research in which a clinical trial on at least a single dose is performed in parallel with performing computer simulation studies using the computer model". It is unclear what is being simulated by using the model? Is the model simulating the clinical research? Clarification is requested.

Claim 1, step (c) recites "adjusting the computer model based upon comparison of the results of the clinical research and the computer simulation". What about the computer simulation is being compared to the clinical research? Are the similarities, differences, or both being compared, for example? Clarification is requested.

Claim 1, step (e) recites "checking the drug for cumulative effects and providing this information to the computer model". It is unclear as to what cumulative effects are being "checked". Clarification is requested.

Claim 1, step (g) recites "determining an optimal protocol for the most responsive patient populations and indications for phase II clinical trial". It is unclear what is intended by this step.

Does applicant intend that the claim read determining an optimal protocol for the most responsive patient populations and indicating a phase II clinical trial based upon some criteria? Clarification is requested.

Claim 1, step (h) recites "performing phase II clinical trial where a number of small scale clinical trials are performed in parallel based upon the results of step g. It is unclear as to what results the claim refers? What results in step g are being used? Clarification is requested.

Claim 1, step (i) recites "analyzing interim results to choose the most promising regimens for continued clinical trials". It is unclear what is intended by "interim results". At what point are results analyzed to choose the most promising regimens? Further, what constitutes a "most promising regimen"? Clarification is requested.

Claim 1, step (j) recites "performing phase III clinical research for chosen indications by chosen protocols". There is insufficient antecedent basis for "chosen indication" and "chosen protocols". Further, what indication and what protocols are intended? Clarification is requested.

Claim 1, step (k) recites "performing phase IV studies for post-marketing subpopulation analysis and long term product safety assessment". It is unclear what the relationship is between the phase IV studies and post marketing and product safety. Clarification is requested.

Claim 2 recites "wherein step b, prior to each sub-step of the phase I trial". There is insufficient antecedent basis in the claim for "each sub-step", as no sub-step is recited in step (b). Clarification is requested.

Claim 2 recites "the computer model is adjusted based upon the comparison". It is unclear as to what about the comparison is used to adjust the computer model. Clarification is requested.

Claim 3 recites "the method of claim 1, wherein a first decision whether to continue with the trial is made, stopping the trial if an adverse decision is made". It is unclear to what "trial" this step pertains. Further, where does this step occur in the claimed method?

Claim 4 recites "the method of claim 1, wherein results of step g are used to define indication and define sub-groups of patients". It is unclear as to what "indications" are intended.

Claim 5 recites "effective treatment protocol". Is in unclear what defines the metes and bounds of "effective treatment". Clarification is requested.

Claim 7 recites "the small clinical trials are performed in parallel for a chosen indication by a chosen treatment protocol". It is unclear as to what "indication" the claim refers. Clarification is requested.

Claim 9 recites "a second decision". This is unclear, as no first decision was determined. Clarification is requested.

Claim 11 recites "efficacy profile". It is unclear what is intended by and "efficacy profile", as no such profile is defined in the specification. Clarification is requested.

Claim 14 recites "the method of claim 1, when hitherto unknown effects are discovered, the computer model is adjusted to obtain predictions for new protocols, patient population, and indication". It is unclear as to when this step is performed within the steps of the claimed method. What predictions are obtained? What indications are indicated? Clarification is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 15-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Iliadis et al. (Computers and Biomedical research (2000) Vol. 33, pages 211-226; PTO 1449 Reference 30).

The instant claims are drawn to a method for performing clinical trials for a new drug comprising performing pre-clinical phase in which a computer model for pk/pd is created; a method for performing clinical trials for a new drug comprising performing phase I clinical trial wherein dose-escalation trial is performed with computer simulation; and a method of performing clinical trials for a new drug comprising developing a strategy for a next sub-step in phase I in conjunction with computer predictions.

Iliadis et al. teach a method in which optimization of cancer treatment is determined by using a mathematical model of pharmacokinetics of anticancer drugs, antitumor efficacy, and drug toxicity (abstract). The first approach relies on modeling to simulate the fate of drug concentration, tumor size, and WBC count (page 218, paragraph 5) (claim 15). The second phase involves protocol implementation, based upon the model (page 218, paragraph 7) (claim 16). The protocols are used clinically, as outlined on page 219. Lastly, optimization of the protocols is performed (page 219, paragraph 5) (claim 17).

No claims are allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

July 27, 2006
Lori A. Clow, Ph.D.
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Lori A. Clow
Patent Examiner